

AD \_\_\_\_\_

Award Number: DAMD17-02-1-0665

TITLE: Neural Mechanisms of Chronic Fatigue Syndrome

PRINCIPAL INVESTIGATOR: Guang H. Yue, Ph.D.

CONTRACTING ORGANIZATION: Cleveland Clinic Foundation  
Cleveland, Ohio 44195

REPORT DATE: April 2003

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command  
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;  
Distribution Unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

20030923 105

REPORT DOCUMENTATION PAGE			Form Approved OMB No. 074-0188	
Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188), Washington, DC 20503				
1. AGENCY USE ONLY (Leave blank)	2. REPORT DATE April 2003	3. REPORT TYPE AND DATES COVERED Annual (1 Apr 02 - 31 Mar 03)		
4. TITLE AND SUBTITLE Neural Mechanisms of Chronic Fatigue Syndrome		5. FUNDING NUMBERS DAMD17-02-1-0665		
6. AUTHOR(S): Guang H. Yue, Ph.D.				
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)  Cleveland Clinic Foundation Cleveland, Ohio 44195  E-Mail: yueg@ccf.org		8. PERFORMING ORGANIZATION REPORT NUMBER		
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)  U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012		10. SPONSORING / MONITORING AGENCY REPORT NUMBER		
11. SUPPLEMENTARY NOTES				
12a. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited			12b. DISTRIBUTION CODE	
<b>13. Abstract (Maximum 200 Words) (abstract should contain no proprietary or confidential information)</b> Nearly one million Americans suffer from chronic fatigue syndrome (CFS). More than 15% of Gulf War veterans (GWV) were found to have CFS. The disease significantly reduces work production of civilian patients and combat ability/readiness of US military forces. Increasing scientific evidence suggests that CFS is a biological illness involving pathology of the central nervous system (CNS). However, little is known about how the CNS is affected by CFS. This study will focus on evaluating brain activities of CFS patients during fatigue and non-fatigue muscle exercises. Our hypothesis is that the brain activation pattern in CFS differs from that of healthy controls. Aim 1 of the study is to determine brain activation patterns during motor activity in CFS patients using functional magnetic resonance imaging. Aim 2 is to examine brain activation patterns during motor activity in CFS patients by analyzing signals of electroencephalograms. Aim 3 is to evaluate signal relationships among different brain regions and between the brain and muscle. Measurements will be made from four groups of participants: a civilian CFS group, a civilian control group, a GWV CFS group, and a GWV control group. We expect that the study will provide objective information for diagnosis of CFS.				
14. SUBJECT TERMS: Chronic Fatigue Syndrome, Gulf War Syndrome, functional MRI, electroencephalogram (EEG), electromyogram (EMG), brain motor activity, brain activation pattern, EEG frequency			15. NUMBER OF PAGES 4	
			16. PRICE CODE	
17. SECURITY CLASSIFICATION OF REPORT Unclassified	18. SECURITY CLASSIFICATION OF THIS PAGE Unclassified	19. SECURITY CLASSIFICATION OF ABSTRACT Unclassified	20. LIMITATION OF ABSTRACT  Unlimited	

## Table of Contents

Cover.....	1
SF 298.....	2
Table of Contents.....	3
Introduction.....	4
Body.....	4
Key Research Accomplishments.....	NA
Reportable Outcomes.....	NA
Conclusions.....	NA
References.....	NA
Appendices.....	NA

## INTRODUCTION

Chronic fatigue syndrome (CFS) is an illness that affects quality of life of both civilian and military populations. However, the diagnosis of CFS is difficult to make because of the absence of specific biomedical markers. Thus, the diagnosis depends primarily on determining whether subjective information provided by the patient meets the clinical case definition of the syndrome. The purpose of this study is to determine whether the central nervous system signals of CFS patients for performing fatigue and non-fatigue motor activities are impaired compared to the signals of healthy volunteers. It is hypothesized that the CNS signals of CFS patients will significantly differ from those of healthy controls. It is expected that at least one or more measurements made by this study will serve as "biological markers" for more objective diagnoses of CFS.

## BODY

This report covers the first year of work related to this study. Up to date, there are still no results available yet. The experiments are under way and we expect to report findings of the study by the midterm or the 2nd-year annual report. The tasks that were performed in the first year include:

- I. *Ordering equipment and supplies.* All pieces of major equipment that were requested have been ordered, tested, and are being used for data collection and analyses.
- II. *Filing IRB (Institutional Review Board) applications.* Three IRB applications were made. Final IRB approval from the principal investigator's institution, the Cleveland Clinic Foundation was obtained shortly after the grant was awarded. The final approval from the Office of Regulatory Compliance and Quality, U.S. Army Medical Research and Materiel Command was given in September 2002. We also filed an application to the IRB Office of Louis Stokes Cleveland Veteran Affairs (VA) Medical Center in order to recruit the Gulf War veterans as research subjects. This application process has been quite long but the final approval is expected to be offered in May 2003. Despite the slow progress of the VA IRB application, and therefore, slow progress of the Gulf War veteran subject recruitment, we have already begun data collection from civilian CFS patients and control subjects (see below).
- III. *Recruiting research subjects.* Twelve civilian CFS patients have been recruited from the Cleveland Clinic and 6 patients has been tested. Ten civilian control subjects have also been recruited and 4 have been tested. More subjects will be recruited in the coming months. We are currently testing more subjects and performing initial data analysis of the tested subjects. We will begin to recruit the Gulf War veteran subjects as soon as the approval from the IRB Office of Louis Stokes Cleveland VA Medical Center is obtained.
- IV. *Data collection and analysis.* As indicated in the last paragraph, we have performed data collection from 10 subjects and begun initial data analysis. We expect that preliminary results will be ready for presentation or publication during near the end of the second year of the project.